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Correspondence arising: Modafinil for cognitive neuroenhancement in health non-sleep-deprived-subjects

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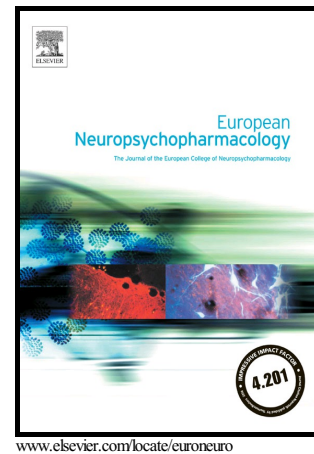
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Letter to the Editor

Correspondence arising: Modafinil for cognitive neuroenhancement in healthy non-sleep-deprived-subjects

The review by Battleday and Brem presents an important update on the effects of modafinil in healthy, non-sleep-deprived individuals while raising crucial methodological concerns about the primary literature being reviewed. However, the review itself has several methodological shortcomings and, in our opinion, fails to comply with the standard systematic review methodology. Relevant articles, e.g. one by Smith et al. (2004), that could have been detected with the applied search terms (modafinil and cognitive), are left out, whereas a study (Ghahremani et al., 2011) that is cited in the review and fulfills the inclusion criteria, is not included in the systematic review. By using solely the two mentioned search terms, the probability of detecting all relevant articles is very limited, and thus, other relevant literature was not included. Further research with a pre-tested, more elaborated search strategy provides several additional relevant articles that should have been reviewed (Stoops et al., 2005; Dodds et al., 2009; Joo et al., 2008; Schmaal et al., 2013). Two of these studies (Smith et al., 2004; Stoops et al., 2005) have already been considered in a previously published systematic review on the same topic (Repantis et al., 2010). Since this review is cited in the article, the authors could have been aware of their existence.

Furthermore, the authors report on the effects of modafinil on mood and provide a percentage of studies assessing mood. Without having defined mood as an outcome of interest for their review and without having specifically searched for trials assessing mood it seems inadequate to comment on this topic because, again, a significant number of articles has been left out. A preliminary literature search reveals at least nine more articles that provide data on effects of modafinil on the mood of healthy individuals. (Warot et al., 1993; Hou et al., 2005; Hou et al., 2007; Samuels et al., 2006; Samuels et al., 2007; Taneja et al., 2007; Volkow et al., 2009) Among these are two studies that were published before 1990 and not taken into account due to an arbitrary time span set by the authors for literature search (Saletu et al., 1989a; 1989b). The same criticism applies to their report on side effects. Finally, the claim that the use of modafinil for neuroenhancement purposes is “extensive” is not being adequately supported. In fact, it is probably not possible to support such a general statement, neither with European nor with U.S. prevalence studies (Maier et al. 2015 – Table 1).

The – mostly null – results that are omitted should be taken into account before stating that modafinil is a “well-validated” nootropic agent. By the same token, methodological limitations, which are reported here to some extent, put the review’s conclusions into perspective. We argue that not only should the ethical issues regarding the use of modafinil for neuroenhancement purposes be a matter of discussion, but that more importantly the question of efficacy and safety of modafinil use by healthy individuals remains unanswered. In fact, the latter question might even be the rate-limiting step in the ethical discussion (Forlini et al., 2013). Therefore, we welcome the recommendations for future studies that the article provides and hope that future research will adequately address this question.

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Conflict of interest

No authors have a financial arrangement with any company or organization that might be a conflict of interest.

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